

Advantages and disadvantages of killed and live poliomyelitis vaccines *

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Decision-making on the use of poliomyelitis vaccines in the WHO Expanded Immunization Programme, and particularly in the developing nations, needs to be based on an understanding of the epidemiology of poliomyelitis in different parts of the globe. Even with two safe and effective kinds of poliomyelitis vaccine available, poliomyelitis has by no means been eradicated from the world. In developed countries that are considered well-vaccinated, certain sectors of the population may be inadequately protected against risk of infection by indigenous or imported wild polioviruses. In developing nations that are in transition toward an epidemic phase of poliomyelitis, wild polioviruses will continue to be a threat until thorough immunization is established and maintained. Killed-virus poliomyelitis vaccines have proved to be effective in certain countries that have used them exclusively; these are small countries with excellent public health systems, where coverage by the killed vaccine has been wide and frequent. Live vaccines, administered to hundreds of millions of persons during the past decade, have also been remarkably safe and effective. However, in certain warm-climate countries induction of antibodies in a satisfactorily high proportion of vaccinees has been difficult to accomplish. The advantages and disadvantages of each kind of poliomyelitis vaccine need to be weighed with respect to the particular setting in which a vaccine has been or will be used.

This article surveys the present situation with regard to poliomyelitis vaccines, and considers particularly aspects that are relevant to the WHO Expanded Programme on Immunization and to the use of these vaccines in developing nations where poliomyelitis may only now be emerging as an important public health problem.

Before discussing vaccines, I shall review briefly some of the basic facts about poliomyelitis and the polioviruses, since understanding of these is fundamental to the wise evaluation of vaccines and vaccine programmes.^a A large proportion of poliovirus infections are completely silent and symptomless. This means that (a) the absence of paralytic cases does not signify that the viruses are absent and (b) a paralytic case can seem to appear out of nowhere, as a solitary event with no obvious source. When persons susceptible to infection are exposed to wild polioviruses, only about 1% of infections result in recognized clinical illness. One of the following responses may occur:

1. Inapparent infection without symptoms.
2. Mild illness (fever, malaise).

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^a WHO Technical Report Series, No. 81 (1954) and No. 145 (1958).

3. Aseptic meningitis. Poliovirus is only one of many viruses that produce aseptic meningitis. A large proportion of aseptic meningitis cases are caused by other enteroviruses (echoviruses and coxsackieviruses), as well as by members of other virus groups.

4. Paralytic poliomyelitis. Paralysis is rare in other enterovirus infections, but may occur. In an analysis of virus isolations reported to WHO from around the world over a 4-year period,^a paralysis was reported in less than 1% of infections by other enteroviruses.

Virus-neutralizing antibody forms within a few days of exposure to the virus, often before the onset of illness, and apparently persists for life. Its formation early in the infection is a result of viral multiplication in the intestinal tract and deep lymphatic structures before invasion of the nervous system. As antibodies must be present in the blood to prevent the dissemination of virus to the brain and are not effective if central nervous system invasion has already occurred, immunization is of value only if it precedes the onset of symptoms referable to the nervous system. Immunity is permanent to the poliovirus type causing the infection.

Passive immunity is transferred from mother to offspring, the maternal antibodies gradually disappearing during the first 6 months of life. Passive antibody (gamma globulin) is effective in preventing paralysis for only one month; it has no effect in preventing poliovirus from infecting and replicating in the enteric tract.

Circulating serum antibody is not the only source of protection against paralytic poliomyelitis. The nature of the so-called local or cellular immunity, which is manifested by protection against intestinal reinfection after recovery from a natural infection or after immunization with live poliomyelitis vaccine, has not been fully elucidated. However, it is increasingly recognized as having an important role in defence against poliovirus infection.

Man is the only known reservoir of polioviruses and close human contact appears to be the primary means of spread. The virus enters by the mouth and primary multiplication takes place at the sites of viral implantation in the oropharynx or intestines. The virus is regularly present in the throat and in the stools before the onset of illness. One week after onset there is little virus in the throat but virus continues to be excreted in the stools for several weeks, even though high antibody levels are present in the blood. Thus faecal contamination is the usual source of infection. However, droplets or aerosols from coughing or sneezing can also be a source of direct or indirect contamination.

Warm weather favours the spread of virus, probably by increasing human contact, the susceptibility of the host, or the dissemination of the virus by nonhuman agents. Polioviruses are readily spread within the family, and the extent of intrafamilial infection appears to be related to the duration of virus shedding, particularly by young children.

EPIDEMIOLOGICAL PATTERNS OF POLIOMYELITIS

Poliomyelitis can be viewed as having three major epidemiological phases: endemic, epidemic, and postvaccination. All of these phases coexist at the present time in different regions of the world.

^a ASSAAD, F. & COCKBURN, W. C. *Bulletin of the World Health Organization*, 46: 329-336 (1972).

Endemic behaviour

In some crowded, developing areas, chiefly in the tropics, paralytic poliomyelitis continues to be a disease of infancy (truly “infantile paralysis”) that is seen only in a rare, sporadic case. In these populations, virtually all children over 4 years of age are already immune. With the almost universal presence of antibody to all three poliovirus types in women of childbearing age, passive immunity is transferred from mother to offspring, and many infants subsequently experience their first poliovirus infections while maternal antibodies still provide some protection. In addition, the ratio of inapparent to apparent infections is highest in infants and young children; thus paralytic disease under these conditions is relatively rare and epidemics do not occur, despite the fact that polioviruses circulate abundantly. In the past, the rarity of clinical poliomyelitis in the tropics had led many to believe that no poliovirus infections were present in such areas, when in fact the reverse was true: polioviruses were highly endemic, but the infections were almost entirely asymptomatic.

In recent years, in a number of instances a high incidence of infantile paralysis has been associated with wide circulation of the virus. In 1974, although there was no evidence of epidemics occurring in the previous few years, the observed prevalence of lameness in Ghana among children of school age was 7 per 1000 and the annual incidence was estimated to be at least 28 per 100 000 population.^a These figures are comparable to those in the USA and Europe prior to the introduction of vaccine.

Behaviour in developed countries

In the developed countries, during the first 50–60 years of the twentieth century, poliomyelitis underwent a transition from the endemic phase to one in which increasingly large and severe epidemics of the paralytic disease occurred. The generally accepted explanation, which has been borne out by numerous studies, is that improved sanitation and hygiene reduced the opportunities for infection among the very young. Therefore, increasing numbers of persons encountered poliovirus for the first time in later childhood or in adult life, at ages when poliovirus infections are more likely to take the paralytic form. The delay in infection also resulted in a build-up of susceptibles in the population to a point at which there was a “critical mass” sufficient to support wide and rapid spread of the viruses. Thus epidemics began to occur, sometimes in an abrupt shift, sometimes after gradual increases in the annual case rates of “sporadic” poliomyelitis. For example, in the USA just before poliomyelitis vaccines became generally available, the annual number of cases of paralytic poliomyelitis ranged from 10 000 to more than 21 000. In epidemics the peak incidence was in 5- to 9-year-old children, and about one third of the cases and two thirds of the deaths occurred in persons over 15 years of age. This was a marked change from the pattern in the great 1916 epidemic, in which approximately 80% of the patients were children under 5 years of age.

In the first half of the twentieth century, not only was it the developed nations that experienced epidemic poliomyelitis, but also it was the socioeconomically advantaged sectors of the populations of these nations that had the largest number of cases. Even within the same city, the wider circulation of polioviruses in areas with poorer sanitation and hygiene provided more children with immunizing infections at an earlier age and

^a OFOSU-AMAAH, S. ET AL. *British medical journal*, 1: 1012-1014 (1977).

reduced their chances of eventually developing paralytic disease.^a The last outbreaks in the USA before vaccine became available include well-off families and a high incidence of paralytic cases occurred among susceptible parents exposed to their virus-carrying children, who themselves might or might not have shown symptoms.^b

Behaviour in the postvaccine era

The postvaccine era for most countries in Europe, North America, and Oceania, as well as some nations in other regions of the world, began after 1955 when killed vaccine was introduced and continued after 1959–1961, when live attenuated vaccines became available on a large scale. These areas experienced a marked reduction in the incidence of poliomyelitis; rarely has a serious disease been controlled so quickly and dramatically. In 1955, 17 364 cases of poliomyelitis were reported in the USSR, 27 343 in the other countries of Europe, and 31 582 in the USA, Canada, Australia, and New Zealand combined—a grand total of more than 76 000 cases. In these same countries in 1967, only 1013 cases were recorded—a reduction of 99% in 12 years. Since 1967, the number of cases has dropped even farther. For example, vaccines have virtually eliminated paralytic poliomyelitis from the United States: from more than 18 000 cases in 1954, the number dropped to about 2500 in 1960 (after killed (Salk-type) vaccines came into general use). After live, oral attenuated (Sabin-type) vaccines were licensed in 1962 and broadly administered in 1963 and subsequent years, the number of paralytic cases continued to decrease—to 31 in 1970, to only 8 in 1975, and to a similar low number in 1976.

Now, in the well-vaccinated areas of the world, postvaccine epidemiological patterns of poliomyelitis are emerging. These patterns differ from one country to another and to some extent even within the same country.

Virus isolation

In a few areas, where repeated mass vaccination campaigns are conducted regularly and are implemented so as to reach virtually all young children, wild polioviruses are rarely identified; almost all poliovirus isolates in these areas now closely resemble the vaccine strains and are generally presumed to be vaccine progeny. Vaccine viruses are abundantly excreted by the vaccinee and infect unvaccinated contacts. The rare cases of poliomyelitis that do appear may be due to imported wild viruses or may in some instances be vaccine-associated. Results of recent studies, for example, suggest that wild polioviruses have been almost completely eradicated from Japan.^c

Breadth of immunity

The success of live poliovirus vaccine programmes in many countries has so substantially reduced the wild poliovirus circulation in these areas that there are now increasing numbers of people whose entire immunological experience with poliovirus is limited to a single vaccine strain of each type. This change in the immunity status of populations has introduced a new question: Is the changed ecological situation acting on wild poliovirus populations as a selective mutational pressure towards wide antigenic divergence from the attenuated vaccine strains? Such antigenic shifts are conceivable, although as yet there is no evidence of any change. If such shifts occur, and if they permit silent circulation of

^a MELNICK, J. L. & LEDINKO, N. *American journal of hygiene*, **54**: 354–382 (1951).

^b MCCARROLL, J. R. ET AL. *American journal of public health*, **45**: 1541–1550 (1955).

^c TAGAYA, I. ET AL. *Bulletin of the World Health Organization*, **48**: 547–554 (1973).

heterologous wild strains to increase, individuals who for some reason lack sufficient vaccine-induced immunity might be at risk of paralytic poliomyelitis. In anticipation of such problems, an appropriate subject for further investigation is whether successive infections with two different attenuated polioviruses of the same type could provide a "broadening" of alimentary tract resistance to wild homotypic viruses.

Behaviour in areas in transition

A changing pattern of occurrence of paralytic poliomyelitis is now being seen in developing countries with rising levels of sanitation, particularly in tropical and semitropical areas. Of 71 tropical and semitropical countries, 45 reported an overall incidence of poliomyelitis in 1966 three times greater than the average annual incidence for the period 1951–1955. In such areas, if comprehensive and regular vaccination programmes are not yet being carried out, outbreaks of paralytic poliomyelitis continue to occur. For example, in Equatorial Guinea, the average annual number of cases was 2 in 1951–1955, 10 in 1961–1965, 12 in 1969, 17 in 1970, and 5 in 1971; an outbreak then occurred in 1972 with a total of 74 cases during that year. A similar trend is being seen in some Central and South American countries. In the years from 1969 to 1973, the endemic level of poliomyelitis in Honduras was reported as being 20–66 cases each year, but in the first 3 months of 1977 there were 109 paralytic cases with 5 deaths. Most of the victims were young children, 73% of them less than 3 years old. Although some vaccine had been used in that country, 72% of the poliomyelitis patients had never received any poliomyelitis vaccine and 19% had received only a single dose. Until immunization programmes are fully implemented to reach the vast majority of populations with sufficient dosage, such areas can anticipate epidemics of paralytic poliomyelitis like those that occurred in the developed countries before vaccines were introduced.

Payne ^a first showed that an inverse relationship existed in many areas between infant mortality rates and the incidence of clinical poliomyelitis. Paul ^b pointed out that when the infant mortality rate in a country drops below 75 per 1000 live births, the incidence of poliomyelitis can be expected to increase. Thus epidemic poliomyelitis was a disease of affluent societies in the first half of the twentieth century and is now an unwelcome concomitant of improved living standards in developing nations unless it is controlled by vaccination.

TRANSITION: CAN WE ANTICIPATE AND FORESTALL THE EPIDEMIC PHASE OF POLIOMYELITIS?

If national health officials and other members of government are aware of the possibility that epidemic poliomyelitis may appear, it should be possible to anticipate and prevent its occurrence. If significant improvements are taking place in hygiene and sanitation and in health facilities, if infant mortality rates are tending to decline, or if there are other changes in conditions that might be relevant (e.g., improved communication and travel), the nation need not and should not wait for a change in poliomyelitis epidemiology

^a PAYNE, A. M.-M. Poliomyelitis as a world problem. In: *Poliomyelitis: Papers and discussions presented at the Third International Poliomyelitis Conference*, Philadelphia, Lippincott, 1955, pp. 393–400.

^b PAUL, J. R. *Bulletin of the World Health Organization*, 19: 747–758 (1958).

to be signalled by the tragedy of paralysed children. Instead, serological surveys for antibody against the polioviruses should be planned and conducted; the tests are not difficult to perform and advice or assistance can readily be obtained from epidemiological and virological experts at WHO or its global network of virus collaborating centres. By testing for neutralizing antibodies in sera from a representative sample of persons living in a region, it is possible to learn the extent of experience the population has had with poliomyelitis, even if there is no historical record of a single paralytic case. Because poliovirus antibodies persist for many years, usually for life, the record can be read in the serological results. It can be determined which virus types were present during any given period, what proportion of the population is immune, and at what ages initial immunizing infections with polioviruses are occurring. Such information is not obtainable from records of epidemics or of clinically recognized and reported cases, since so large a proportion of poliovirus infections are inapparent. Furthermore, the first paralytic cases occurring in a region may not be recognized as poliomyelitis because the disease has not been seen in the district and health personnel are not accustomed to considering poliomyelitis as a possible diagnosis.

In planning a serological survey, it is vitally important that all sectors of the population be included. Population subgroups within a nation may be widely divergent in health practices and life-styles, and hence in the age at which children are naturally exposed to polioviruses. This was illustrated in the USA in the years before vaccines were available: in a poorer district of one city that we studied, 62% of the children 1-4 years old already had antibodies to at least one poliovirus serotype, while in a better-off area of the same city only 42% of this age group had antibody to any poliovirus. Among the older children (10-14 years), 96% of the poorer group but only 66% of the better-off group had antibody to at least one poliovirus type. In addition to factors of hygiene or living standards, the cultural or geographical isolation of young children in some sectors of a population may also affect the tendency for an individual's initial experience with polioviruses to be delayed.

If the serological survey demonstrates that an appreciable part of the population remains susceptible into later childhood, serious consideration must be given to instituting a full-scale immunization programme so that poliomyelitis epidemics never have a chance to take place.

For current poliomyelitis immunization programmes also, periodic serological surveys are important for monitoring the maintenance of protection. They can indicate whether significant proportions of the susceptible age groups are being reached and protected by vaccination, and whether antibody distribution parallels the estimates of immunity based on surveys of vaccination history. It is also important to determine the persistence of vaccine-induced antibodies over the years.

In 1957, Payne ^a drew attention to the fact that clinical surveys of residual paralysis in young children of preschool or school age can provide valuable information on the incidence of poliomyelitis. The sequelae of paralytic poliomyelitis are distinctive and can be attributed to poliomyelitis with a high degree of reliability. A survey of lameness among children of school age in Ghana in 1974 provided accurate information on the disease problem in both rural and urban communities.^{b,c} It would therefore seem that simple

^a PAYNE, A. M.-M. In: *Poliomyelitis: Papers and discussions presented at the Fourth International Poliomyelitis Conference*. Philadelphia, Lippincott, 1957, pp. 157-164.

^b NICHOLAS, D. D. ET AL. *British medical journal*, 1: 1009-1012 (1977).

^c OFOSU-AMAAH, S. ET AL. *British medical journal*, 1: 1012-1014 (1977).

clinical surveys have a definite place in assessing the magnitude of the problem in the community.

POLIOMYELITIS VACCINES

In this discussion of poliomyelitis vaccines, "killed poliomyelitis vaccine" refers to vaccine prepared from killed poliovirus (Salk type) and "live poliomyelitis vaccine" refers to vaccine prepared from living attenuated strains of poliovirus (Sabin type).

With two effective kinds of vaccine available, the killed vaccine administered by injection and the live vaccine administered orally, how does an individual, a physician, or a nation decide which should be used for which purposes? There are advantages and disadvantages, risks and benefits, with either the killed or the live vaccine.

No medical intervention of any sort is absolutely risk-free. Even the commonest drug may carry some degree of risk to a fairly large number of users, and a possibly life-threatening risk to an exceedingly small number of persons who are hypersensitive to it. Any public health or medical judgment must be made on the basis of balancing the values and the problems of one procedure against those of another procedure and against the risks of doing nothing at all.

Both live and killed poliomyelitis virus vaccines have been used widely and have been both safe and effective in the past 20 years. Nevertheless, a healthy respect should be maintained for the polioviruses used as vaccine sources and great care must be exercised by those undertaking the manufacture or the administration of either vaccine.

Killed vaccine

Vaccine inactivated by formalin is prepared from polioviruses grown in monkey kidney cultures. Starting in 1955, it was extensively used to inoculate children in many countries that were suffering from severe epidemic poliomyelitis at that time. As Sabin^a has aptly stated: "The development by Jonas Salk of an effective formalinized vaccine provided a tool with which the incidence of the paralytic disease could be greatly reduced and many thousands of paralytic cases had been prevented by its use in various parts of the world."

Inactivated poliomyelitis vaccine is used in Finland, Sweden, Holland, and some parts of Canada. For primary immunization, four inoculations are required, the first three at 4- to 6-week intervals and the fourth 6-12 months later. A booster dose has generally been considered necessary every few years in order to maintain immunity. The advantages and problems of killed poliomyelitis vaccine are summarized in Table 1, and are discussed below.

Advantages of killed vaccine

Properly prepared and administered, killed vaccine induces good levels of humoral antibodies in a satisfactory proportion of those receiving sufficient dosage, and thus protects the vaccinee against paralytic poliomyelitis. It can also provide sufficient protection to whole populations and is believed to have limited the circulation of polioviruses in several nations that use it. It contains no living virus and therefore cannot mutate towards increasing virulence. Because living virus is absent, it is safe to administer killed vaccine (a) to persons with immune deficiency diseases and their families and (b) to persons

^a SABIN, A. B. *Journal of the American Medical Association*, 194: 872-876 (1965).

Table 1. Killed poliomyelitis vaccine: advantages and problems

Advantages	Problems
1. Confers humoral immunity in a satisfactory proportion of vaccinees if a sufficient number of doses are given.	1. Several studies have indicated a disappointing record in the percentage of vaccinees developing antibody after three doses. ^a
2. Can be incorporated into regular paediatric immunization with other vaccines (DPT).	2. Generally, repeated boosters have been required to maintain detectable antibody levels. ^a
3. Absence of living virus precludes potential mutation and reversion to virulence.	3. Does not induce local (intestinal) immunity in the vaccinee.
4. Absence of living virus permits its use in immunodeficient or immunosuppressed individuals and their households.	4. More costly than live vaccine.
5. Appears to have greatly reduced the spread of polio-viruses in small countries where it has been properly used (wide and frequent coverage).	5. Subject to problems raised by the growing scarcity of monkeys.
6. May prove especially useful in certain tropical areas where live vaccine has failed to "take" in young infants.	6. Use of virulent polioviruses as vaccine seed could lead to tragedy if a failure in virus inactivation were to occur.

^a Some of the disappointing results in the decade after killed vaccine was introduced may have been due in part to problems that have now been corrected.

undergoing immunosuppressive therapy or others recognized as having some special problems in dealing with living agents of disease. Killed vaccine might be combined with diphtheria-pertussis-tetanus vaccines and incorporated into an immunization schedule for infants and young children. Such a combination programme of "quadruple" vaccine administration can be especially helpful in certain tropical areas where there have been failures of live poliomyelitis vaccine to "take" in infants (see page 36). Although the killed-virus vaccine may not confer intestinal resistance to carriage and spread of virulent live virus in the community, the neutralizing antibody it elicits would provide protection against paralysis even if vaccinated children were to become infected with a wild virus. On a philosophical level, it has the advantage of not introducing into the community any living virus that can spread in an uncontrolled fashion to persons other than those who have sought or agreed to receive the live vaccine.

Problems associated with the use of killed vaccine

The licensing of killed vaccine was preceded by an immense nationwide trial in the USA, in which vaccine was administered to several hundred thousand children. Yet immediately after the success of the trial had been reported and the vaccine licensed, 61 cases of paralytic poliomyelitis appeared in vaccine recipients and 80 cases in their family contacts.

These cases were epidemiologically linked to certain lots of vaccine subsequently found to contain small amounts of live, virulent poliovirus that had been undetected by the manufacturer. The breakdown in safety procedures that allowed the live virus to remain in the final vaccine was due to problems of transferring laboratory procedures to manufacturing production processes, particularly of extrapolating inactivation data. These problems were resolved and there have been no further reports of any residual live-virus problems with any inactivated poliomyelitis vaccines manufactured according to well standardized procedures.

Following the use of killed vaccine, the incidence of paralytic poliomyelitis was greatly reduced. However, a few localized epidemics continued to occur, mostly among unvac-

inated children. However, some cases also occurred among the vaccinated; in a study of several thousand paralytic cases, 17% were in triple-vaccinated children and in 1960, despite the extensive use of inactivated vaccine for almost 5 years, there were still more than 2500 paralytic cases reported in the United States. Some of the disappointing results may have been due primarily to problems that now have been corrected in the areas still using inactivated vaccines. For example, after the early manufacturing defect, additional safety precautions (an extra filtration step) reduced the virus concentration, and consequently the potency, of the vaccine during the period 1956–1958.

Killed vaccines have usually required continued administration of booster doses at various intervals. This situation is conducive to a decline of immunity levels in the population over a period of time because families, and also public health workers and physicians, may neglect or overlook the required booster schedule. Booster doses also add to the cost of the vaccine and its administration.

In Sweden and Finland and in two provinces of Canada (Ontario and Nova Scotia), the current poliomyelitis immunization programmes rely on killed vaccine alone. In 1969 and 1970, a survey was made in Ontario, in some of the areas where immunization with killed vaccine had begun in 1955 and where a mass campaign with live vaccine had been conducted in the schools in 1962 but had not been repeated. Among the children 4–6 years old (i.e., those not born at the time of the single 1962 live-vaccine campaign and hence dependent on the killed vaccine for their immunization), only 65% had antibodies to all three types of poliovirus; even among children who had received six or more doses, only 74% had antibodies to all three poliovirus types. The effect of one or two doses of live vaccine in addition to killed vaccine was found to be highly significant: antibodies to all three types of poliovirus were found in virtually all children who had received both kinds of vaccine. The investigators (who included manufacturers of the killed vaccine) concluded their report by predicting that immunity in the school-age population would decline to a dangerous level unless live vaccine were used after immunization with killed vaccine.^a

One of the arguments often presented for the use of killed-virus vaccine is that, although serum antibody may be at very low or even undetectable levels, there is an enduring “immunological memory”. This state, not measured by antibody tests, is said to enable the vaccinee to make a very quick and high-titre antibody response on further exposure to the virus.^b Lack of serum antibody indeed may not indicate complete lack of protection against clinical illness. However, serum antibodies do contribute to the prevention of viraemia and therefore minimize the possibility that the nervous system will be invaded. It is therefore risky to assume that protection exists when serum antibody cannot be demonstrated.

Another problem associated with immunity following the administration of killed poliomyelitis vaccine is that, although humoral antibodies are induced, local (intestinal) immunity is not. Hence, wild polioviruses can still multiply in the intestinal tract of the vaccinee and be a source of infection to others.

Recent reports indicate that killed vaccine alone can provide sufficient protection to whole populations, but I would emphasize that these reports are from small countries with excellent national health programmes that cover the entire population and ensure administration of full primary vaccination and frequent boosting. In Finland and Sweden up to

^a MACLEOD, D. R. E. ET AL. *Canadian Medical Association Journal*, 113: 619-623 (1975).

^b SALK, J. & SALK, D. *Science*, 195: 834-847 (1977).

1977, no paralytic poliomyelitis had been reported for over a decade. It has been suggested that the reason so little poliovirus has been found in Finland and Sweden is that they are adjacent to countries where live vaccine continues to be widely distributed and that opportunities for the importation of wild polioviruses are thus reduced. However, early in 1977 two cases occurred in Sweden and a number of poliovirus carriers were detected in the area. The patients had no history of vaccination; this was also true of most of the carriers.

The fact that there has been no other accident of manufacture such as occurred when the killed vaccine was first licensed in the USA should not lead to recklessness or complacency. Although killed vaccine has been in use for more than 20 years, the number of persons who have received it, particularly after 1961, has been relatively limited compared to the many hundreds of millions who have received live vaccine. If vastly greater numbers of doses of killed vaccine were to be used, requiring many additional producers, the chances of an unfortunate accident might well be increased. Virulent seed viruses are still used for preparing the killed poliovaccines and single break in the chain of safety procedures could lead to an enormous tragedy. In this respect, to paraphrase Santayana, we do well to remember the past—in order that we be not condemned to repeat it.

Future possibilities

If a killed vaccine for poliomyelitis is wanted, one wise course would be to start with an attenuated strain for the seed virus. Then, if production and testing accidents should occur and the recipients were accidentally *injected* with live poliovirus, at least the number of poliomyelitis cases produced would be fewer.

Some new techniques are being explored towards improving killed-virus vaccines. One approach has been to obtain a very high concentration of virus, purify it, and then prepare a subunit vaccine that contains no viral nucleic acid but only selected polypeptides that are antigenically active. This would not really be a killed-virus vaccine but an alternative to either killed-virus or live-virus vaccines. It would be a vaccine made up of a purified antigenic component, containing virtually no extraneous material except the precise components needed to stimulate good immunity. Just such a polypeptide preparation is being studied in one of the promising approaches to a vaccine against viral hepatitis B.

Live vaccine

During 1952–1955, live virus vaccine candidates, attenuated by serial passage in tissue culture, were developed by a number of workers. These efforts came to fruition in 1955–1959 and large-scale field trials were held in many countries under a variety of conditions; 20 vaccination campaigns in 15 countries were reported at the First International Conference on Live Poliovirus Vaccines in 1959 and additional campaigns were described at the Second International Conference in 1960.^a Routine use of live poliomyelitis vaccines was begun in many countries during the spring of 1960 and vaccines made from the Sabin strains were licensed in the USA in 1961–1962. In the early years of live vaccine immunization, monovalent vaccines incorporating each serotype separately were the most commonly used, but trivalent vaccine is now used widely. With trivalent vaccine, the primary immunization schedule calls for the first dose of vaccine to be given at 2 months of age; the second and third doses are given at 2-month intervals thereafter and a fourth dose

^a Pan American Health Organization Scientific Publication No. 44 (1959) and No. 50 (1960).

Table 2. Live poliomyelitis vaccine: advantages and problems

Advantages	Problems
<ol style="list-style-type: none"> 1. Confers both humoral and intestinal immunity, like natural infection. 2. Immunity induced may be lifelong. 3. Induces antibody very quickly in a large proportion of vaccinees. 4. Oral administration is more acceptable to vaccinees than injection, and easier to accomplish. 5. Administration does not require the use of highly trained personnel. 6. When stabilized, can retain potency under difficult field conditions with little refrigeration and no freezing. 7. Under epidemic conditions, not only induces antibody quickly but also rapidly infects the alimentary tract, blocking spread of the epidemic virus. 8. Is relatively inexpensive, both to produce the vaccine itself and to administer it, and does not require continued booster doses. 9. Can be prepared in human cells and is therefore not dependent on continuing large supplies of scarce monkeys. This also eliminates the theoretical risk of including monkey virus contaminants in the vaccine. 	<ol style="list-style-type: none"> 1. Being living viruses, the vaccine viruses do mutate, and in rare instances have reverted toward neurovirulence sufficiently to cause paralytic poliomyelitis in recipients or their contacts. 2. Vaccine progeny virus spreads to household contacts.^a 3. Vaccine progeny virus also spreads to persons in the community who have not agreed to be vaccinated.^a 4. In certain warm-climate countries, induction of antibodies in a satisfactorily high proportion of vaccinees has been difficult to accomplish unless repeated doses are administered. In some areas, even repeated administration has not been effective. 5. Contraindicated in those with immunodeficiency diseases and their household associates, as well as in persons undergoing immunosuppressive therapy.

^a Some people consider this spread into the community to be an advantage, but the progeny virus excreted and spread by vaccinees is often a mutated virus. Obviously it cannot be a safety-tested vaccine, licensed for use in the general population.

is given at 18 months of age. A booster is given at about 6 years of age and no further boosters are considered necessary under most conditions. The advantages and problems of the use of live poliomyelitis vaccines are summarized in Table 2 and are discussed below.

Advantages of live attenuated vaccine

This vaccine is given by the oral route. It **infects**, multiplies, and thus immunizes. In simulating the natural poliovirus infection, **it confers long-lasting** (possibly even **lifelong**) immunity. Like the natural infection, **infection with the vaccine viruses** not only **stimulates** circulating antibody but also induces a state **of resistance of the intestinal tract, which tends** to block the spread of circulating virus in the **community**. **Under normal conditions**, booster doses are seldom needed. Since the live vaccine **is given orally, it is easy** and inexpensive to administer and is more acceptable in many populations. **It is also much less** expensive than the inactivated vaccine, both in terms of single-dose **costs and administration** and in terms of the total amount needed to establish and **maintain adequate immunity**.

For use in warm countries under conditions of mass administration, and in remote field clinics where refrigeration is limited or nonexistent, stabilizers are **available** to protect the potency of live poliovirus vaccines against thermal inactivation. Although the stabilizing effect of magnesium chloride is greater than that of sucrose at high temperatures (over 40°C) and for long periods of time (such as a month),^a sucrose is reported to be protective for about a week in tropical regions with ambient temperatures of 30–35°C. If the vaccine is stabilized with magnesium chloride, it should be kept in tightly stoppered vials in order

^a MELNICK, J. L. ET AL.: *Journal of the American Medical Association*, **185**: 406-408 (1963).

to prevent the pH from rising above 7.0. If the pH remains above 7.0, the stabilizing effect is lessened. This pH effect does not occur with sucrose.

In the face of a poliomyelitis epidemic, live vaccine can be easily administered and quickly stimulates immunity, thus halting the epidemic.^a In addition, because the live vaccine viruses become established quickly in the alimentary tract of the vaccine recipients, they are capable of blocking infection with epidemic virus strains within a matter of days, even before the vaccine-induced antibody becomes fully effective.

Because it is orally administered, live vaccine is also more practical for mass administration and it can be readily taken to remote areas and given rapidly without requiring the services of large numbers of skilled personnel.

Another advantage of live vaccine is that it does not depend on a supply of scarce monkeys. Initially, oral poliomyelitis vaccine was prepared in monkey kidney cell cultures but more recently human diploid cell cultures have been used, and human diploid cell lines are now licensed for vaccine production. This is desirable because of the possibility that the supply of suitable monkeys may be greatly curtailed. Also, the use of monkey tissues carries possible hazards (unknown viral contaminants such as the dangerous Marburg virus, for example) that would not exist with human cells. The most thoroughly studied human diploid cell lines are WI-38 and MRC-5; these cells have been found free of microbial contamination and can be held frozen until needed for vaccine production. Safety testing of such a cell stock can be far more complete than the testing that is possible within the relatively brief life span of primary cultures such as those from monkey kidney.

Problems with live vaccines

While the spread of live vaccine virus from the vaccinee to household and community contacts is considered by some to be an advantage, in that it may provide "free immunization" to larger numbers of persons, the fact remains that the virus that spreads to the contacts is not a licensed vaccine. Vaccine virus progeny excreted by the vaccinees is known to mutate, and it is theoretically possible that it could revert sufficiently toward neurovirulence to cause paralytic poliomyelitis in the contacts of the vaccinee. All strains of poliovirus, regardless of how highly attenuated, retain the property of multiplying in and destroying cells in the monkey spinal cord—the crucial test used to determine whether a strain is sufficiently attenuated and safe for vaccine use. The degree to which monkey neurotropism is retained, however, varies over an enormous (millionfold) range from the virulent strains to the highly attenuated ones suitable for vaccine seed. The techniques used in recognizing and certifying vaccine strains for safety are such that different degrees of neurotropism, even among attenuated strains, can be detected. For example, it has been found that vaccine progeny virus after multiplication in the vaccinees, although still attenuated, would no longer pass the safety tests required of the vaccine itself. The viruses, particularly type 3, do mutate in the course of their multiplication in vaccinated children and rare cases of paralytic poliomyelitis have occurred in recipients or in their close contacts. It is for this reason that many authorities recommend that, when a developed nation or region begins administration of oral poliomyelitis vaccines, the initial programme should be conducted in intensive campaigns designed for mass immunization of the entire population of an area at the same time; thus the polioviruses that would infect virtually the entire population of all ages would be the certified and tested vaccine viruses themselves

^a YOFFE, J. ET AL. *American journal of hygiene*, 76: 225-238 (1962).

rather than untested progeny viruses excreted by vaccinees. At the minimum, all susceptible members of a family should be vaccinated simultaneously. Community vaccination also should be done at a time of year when the prevalence of enteroviruses is at a minimum, to avoid blocking of vaccine virus "takes" by viral interference. Once the bulk of the population in an area has been immunized, subsequent routine immunizations can be limited to babies and young children. This procedure should be sufficient, so long as a large proportion of the children (80–90%) do indeed receive the complete course.

When a developing country begins administration of oral poliomyelitis vaccine, the initial programme should be conducted in intensive campaigns designed to immunize the entire child population of 3–24 months of age at the same time. If serological surveys or clinical disease indicate risk to younger^a or older children, the age limits of the populations to be vaccinated may be altered accordingly, from 1 to 36 months of age.

Some advantage does come from the spread of vaccine virus to unvaccinated contacts, as can be seen from the higher degree of population protection against wild polioviruses than would be expected on the basis of vaccination histories. In the USA in recent years, there has been a disturbing decline in the rates at which some of the important childhood vaccines, including measles and poliomyelitis vaccines, are being delivered to the population. (For example, among children 1–4 years of age, those lacking adequate immunization against poliomyelitis in 1974 ranged, in various population sectors, from 33% to 55%). The incidence of measles has increased greatly following this decline in vaccination delivery, but no such increased incidence has occurred with poliomyelitis, and the numbers of poliomyelitis cases continue to be exceedingly low—less than 10 per year since 1973. The circulation of wild polioviruses, known to be imported regularly and chiefly from Mexico, seems to have been effectively blocked, an effect consonant with greater population immunity than could be expected from the numbers of vaccinees alone.

Epidemiological data obtained in the USA and elsewhere indicate that the instances in which the live vaccine virus has reverted to neurovirulence and attacked vaccinees or their close contacts are exceedingly rare. Recently, in the USA, new discussions and arguments have arisen from proposals that killed vaccines be re-established for general use in that country. The argument for killed vaccines has included reference to the "dangers" of the live vaccine. Because of unfortunate distortions by the news media and their possible effects on public reaction, I would like to re-emphasize what has repeatedly been stated by many different national and international groups of experts: a vaccine that in the USA produces, at most, one case per 11.5 million vaccinees (and one case per 3.9 million contacts) is far from "dangerous" but rather is outstandingly safe, as well as effective. Furthermore, the actual number of vaccine-induced cases is probably even smaller than these figures indicate, for the assignment of "vaccine-associated" status to a paralytic case means only that, on the basis of the temporal relation of vaccination and onset, the vaccine *cannot be ruled out* as a possible cause.

Because of the need to monitor the characteristics of polioviruses isolated from persons who have received live vaccine, and particularly from those few who develop paralytic poliomyelitis or whose contacts develop poliomyelitis, there have been many efforts to design laboratory tests capable of indicating whether a poliovirus isolate is vaccine-derived or a wild virus. A number of such "marker" tests have been used but their results cannot give absolute answers and some investigators consider them of little help, at least in

^a MELNICK, J. L. Unpublished report to WHO, 1977.

deciding whether a particular case of poliomyelitis is vaccine-derived. They can contribute towards designating a particular virus excreted by a vaccinee or a contact as "vaccine-like" or "non-vaccine-like", but the former does not necessarily mean that the virus was derived from the vaccine virus, for there are wild polioviruses with similar "marker" properties. Results of the currently available marker tests cannot, by themselves, indicate whether vaccine virus progeny caused the illness; at best, such markers can be used only by highly experienced investigators, together with other information about the history of a particular poliomyelitis case, to make an informed judgement as to whether the case was "probably vaccine-caused" or "probably caused by a wild virus". As regards distinguishing virulent strains (whether vaccine-derived or wild), the monkey neurovirulence test, conducted by inoculating monkeys and evaluating the results according to precise and standardized procedures, is the only test that can truly distinguish virulent and attenuated strains.

A detailed study has been under way since 1969, conducted by a special committee established by the World Health Organization and specifically charged "to investigate the possible relationship between acute persisting spinal paralysis and the use of poliomyelitis vaccine (oral)". In reporting recently on the first 5 years of their studies, the group stated: "The findings of this report confirm . . . that poliomyelitis vaccines (oral) made from the Sabin attenuated strains are among the safest vaccines in use today . . ." ^a

In an evaluation of the study, a coherent picture has begun to emerge, despite different methods of investigation and reporting among the participating countries. During the first 5 years of the study, 360 cases of paralytic poliomyelitis were assessed; 155 were classed as "no known contact" and appeared to have been due to wild viruses still circulating in these communities. In the participating countries, in which more than 191 million doses of vaccine were given during the period under review, there remained 205 cases that had at least a possible association with live poliomyelitis vaccines. Direct calculation of the risk of vaccination to recipients and their contacts cannot be made since this would require data on both the number of doses actually received and the number of susceptible (antibody-free) people in contact with vaccinees. Nevertheless, some estimate may be made of the occurrence of persistent paralysis in relation to vaccine, based on rates per million doses distributed. There were considerable differences from one country to another. Two countries had no recipient cases, and in the others the rates in recipients per million doses distributed were: 0.087, 0.208, 0.314, 0.390, 1.379, and 2.288. Contact and possible contact cases ranged from 0.135 per million doses up to 0.645, except in two high-incidence countries (see below), which reported 3.305 and 8.046. The most striking finding was the high association with type 3 virus in the recipient cases and with type 2 virus in the contact and possible contact cases. In all countries, most of the cases in the recipient groups occurred in children under 5 years of age, but in the contact groups there was a difference in the age-grouping of the cases between short-campaign countries and countries conducting vaccination throughout the year: in the countries vaccinating throughout the year, many of the contact cases occurred in the nonimmune parents of recently vaccinated infants, whereas in the short-campaign countries most such cases occurred in children under 5 years of age. This difference is attributed to the fact that in the short-campaign countries, (a) there has been a concentration of effort over short periods to ensure good coverage of susceptible children, (b) vaccination has been in progress for 15 years, and

^a *Bulletin of the World Health Organization*, 53: 319-331 (1976).

(c) the adult populations are also well immunized, so that the only susceptible persons would be infants and young children. In the countries offering vaccination throughout the year without intensive campaigns, however, the coverage—particularly in the older age groups—was not so complete; hence parents could be susceptible and could become infected with virus excreted by their own vaccinated children.

Two countries had by far the highest incidence of cases in both recipients and contacts. Exhaustive examination of many factors that might account for these differences has suggested that part of the explanation lies in the quality of the vaccine. During the early years of the study, these two high-incidence countries (together with one other study country) were using vaccine from the same source, without continuous external control, and were using seed viruses at high passage levels. The situation changed during the enquiry and the incidence of paralytic cases decreased.

In addition to re-emphasizing the remarkable safety of the live poliomyelitis vaccines, the enquiry has pointed out that:

“... the differences between the experience of different countries suggests strongly that the very greatest care is necessary in the continuation of intensive surveillance of vaccination and in the preparation and testing of the seed viruses as well as of the vaccines produced from them. All vaccines should comply in all details with the WHO Requirements^a or similarly stringent national requirements. Any change in production methods, or in seeds or substrates, should be regarded as giving rise to new vaccines that must be introduced into populations gradually until it has been shown that the change in production has not altered the safety of the vaccine. By far the most important factor is consistency of production and in order to establish this, control in the laboratory and in the field of a number of batches of vaccine is essential.”

In warm-climate countries, there is some evidence that live poliomyelitis vaccines do not induce antibody production in as high a proportion of vaccinees as in areas with more temperate climates. This lower rate of vaccine “take” has been ascribed to various possible factors, including interference from other enteric viruses already present in the intestinal tract. Interference can be an important problem in warm-climate areas where enteroviruses are abundant. For example, in a study of infants in Karachi, Pakistan, almost all of whom were less than 2 years old, approximately 80% yielded at least one enterovirus in the alimentary tract.^b Mixed infections may also occur in children living in developed countries, but they are far less frequent. Other factors that have been suggested as possibly responsible for this problem are: the presence of antibody in breast milk; the presence of cellular resistance in the intestinal tract owing to previous exposure to naturally circulating polioviruses (or perhaps related viruses); protein deficiency; or the presence of an inhibitor in the alimentary tract (saliva) of infants in these areas that acts against multiplication of the vaccine virus.^c

A recent WHO field study conducted in Africa^d confirmed previous reports on the inhibitor in infants' saliva and indicated that it may have a greater effect than interfering viruses in decreasing implantation and/or multiplication of the vaccine virus. The inhibitor was neutralized by antibodies present in horse serum prepared against human gamma globulin; the oral administration of this serum together with the vaccine virus increased the seroconversion and vaccine virus excretion rates. However, the duration of vaccine virus excretion was limited and the antibody levels elicited were low. Further studies of the

^a WHO Technical Report Series, No. 486, 1972, pp. 20-58.

^b PARKS, W. P. ET AL. *American journal of epidemiology*, **85**: 469-478 (1967).

^c COCKBURN, W. C. & DROZDOV, S. G. *Bulletin of the World Health Organization*, **42**: 405-417 (1970).

^d DÖMÖK, I. ET AL. *Bulletin of the World Health Organization*, **51**: 333-347 (1974).

inhibitor are desirable and are under way. In a small group of children in India,^a extremely high doses (10 times standard) of monovalent oral poliomyelitis vaccines have been administered in efforts to overcome the inhibition problem. While the rates of seroconversion were slightly better, the authors concluded that, in view of the relative inconvenience of administering monovalent vaccine and because it was hypothetically possible that the risk might be increased by administering so high a dosage of live virus, the use of repeated doses of standard trivalent vaccine would be more feasible, with virtually as good an effect.

For the present, practical experience has shown that a high level of population immunity can be achieved in some warm-climate countries by the use of repeated doses of standard live vaccine alone, if given on a regular basis to infants and young children. Furthermore, live vaccine has been shown to be as effective a means of cutting short an epidemic in a warm-climate country as it is in a temperate-climate country when given, preferably in repeated doses, to a high proportion of the presumed susceptible population in an epidemic area.^{b,c} However, in certain areas where multiple doses of live vaccine have not succeeded in adequately immunizing infants, a programme for inoculation of killed vaccine, or for killed vaccine together with scheduled feedings of live vaccine, should be considered for use until this special problem can be overcome.^d

In evaluating vaccine-associated cases and also in making recommendations for vaccination, it is important to emphasize the hazards of administering live vaccines to persons with immune-system disorders. Previously, it had been thought that poliomyelitis immunization with live vaccine might be safely attempted in individuals with humoral immunodeficiencies, although not in those whose cellular immune system was defective. However, it has been recognized recently that live poliomyelitis vaccine should not be used if either cellular or humoral immunity is impaired. It has been recommended, therefore, that for infants and children with such immune deficiency diseases and for their siblings, killed poliovirus can be used (although its prophylactic efficiency in such a child may be limited by the child's immunodeficient state).

Persons who are scheduled for treatment with immunosuppressive drugs constitute another group who need special consideration with regard to live-virus immunization, and these individuals are increasing in number with the growing success of cancer chemotherapy. Such persons, unless they already have antibodies to all three types of poliovirus, should be immunized before their immunosuppressive therapy begins.

In the USA during 1961–1971, there were 73 poliomyelitis cases among vaccine recipients and 37 cases among contacts. Nearly 10% of these cases were in persons with immune-system disorders, an incidence almost 10 000 times greater than in normal persons. Cases in persons with immune deficiency diseases have continued to be reported: during 1975 and 1976, seven such patients were identified.

Without discounting the tragedy involved for the individual child and family who suffer in the exceedingly rare instance when an immunodeficient individual encounters and succumbs to vaccine or progeny poliovirus, it must be recognized that some of these children are notoriously subject to infection, which is frequently fatal, by a wide variety of normally benign or avirulent agents. Clearly, if immunodeficiencies are known or even suspected in potential vaccinees or their siblings, live poliomyelitis vaccine should not be

^a JOHN, T. J. ET AL. *Bulletin of the World Health Organization*, **54**: 115-117 (1976).

^b COCKBURN, W. C. & DROZDOV, S. G. *Bulletin of the World Health Organization*, **42**: 405-417 (1970).

^c YOFE, J. ET AL. *American journal of hygiene*, **76**: 225-238 (1962).

^d MELNICK, J.L. Unpublished report to WHO, 1977.

administered. However, unless other circumstances have brought the condition to light, such immune-system problems may remain undetected by the time the first routine vaccine doses are given at about 2 months of age.

CONCLUDING REMARKS

Even with two kinds of poliomyelitis vaccine available, poliomyelitis has by no means been eradicated. There is reason to believe that, even in well-vaccinated countries, there are still pockets of the population in which wild polioviruses circulate; furthermore, virulent wild polioviruses are still endemic in many parts of the world and importations can easily occur. In well-vaccinated nations, if complacency allows the population to become susceptible because of failure to administer vaccine, wild polioviruses will again become a danger. Furthermore, because a large proportion of poliovirus infections are silent and subclinical, imported viruses could become widely disseminated before the first sign of their presence appeared in the form of a paralysed child or adult. If a nation's population is entering its epidemic period of poliomyelitis, wild polioviruses will continue to be a threat to health until broad and thorough immunization programmes are instituted and maintained.

Since killed vaccine has proved to be effective in preventing poliomyelitis outbreaks in such small countries as Sweden and Finland, there seems to be no reason to change such programmes. By the same token, since live vaccines have been working superbly for 15 years in the USA, USSR, and many other countries around the world, it would be unwise to interfere with these programmes. It is difficult to see what public health purpose would be served by some proposals now being promulgated for offering killed vaccine as an alternative choice for the general population in the USA. It seems likely that a propaganda campaign for killed vaccine (which would magnify the so-called failures of the live vaccine) would merely make people hesitate about accepting any poliomyelitis vaccine, and thus would increase the ranks of those who lack any protection against poliomyelitis. If a national health service elected to change from live to killed vaccine, then a new and untried situation would exist in that country's defences against poliomyelitis, and urgent new questions would be raised that have never been fully answered in the particular national settings concerned, especially in nations having voluntary health systems: Would individuals maintain their immunity adequately by returning for repeated booster injections? Would killed-vaccine-induced immunity, even if sufficient to protect the individual from paralytic poliomyelitis be able to block the circulation of wild viruses as effectively as the live vaccine? Would the extra costs for vaccine, for its administration, and for repeated boosting be justified? Since the live vaccine already in use has proved to be highly effective and safe, are there not other health programmes far more urgently in need of funds? It seems probable that most developing nations instituting their first poliomyelitis immunization programmes would choose live vaccines, if only for economic and logistic reasons. However, if they did choose killed vaccine instead they, too, would need to deal with many of the questions raised above.

Nations engaged or about to be engaged in large vaccination campaigns need to consider the legal as well as the moral responsibilities of such large health programmes, which inevitably carry some degree of risk. Recent experiences in the USA have included the possible association of Guillain-Barré syndrome with the 1976 inactivated swine influenza vaccine; other vaccines and injections might also be involved in this rare and

little-understood disease. A few years earlier, vaccine manufacturers had begun to question the wisdom of continuing production because of enormous liability suits and penalties resulting from rare reactions to vaccine prepared strictly according to all regulations promulgated by the government and meeting all safety requirements. A number of companies in the USA and the United Kingdom have abandoned vaccine production. In an effort to deal with this problem, some vaccinees or their guardians have been required to sign an "informed consent" form but this is rather meaningless and is often merely a way to shed responsibility, since the form describes risks that cannot be readily understood or evaluated by most lay persons. A procedure recently recommended in the USA, by which the recipient not only agrees but also expresses a wish to participate in the vaccination programme, may go some way towards solving this problem.

A vastly more important factor is the development of true public understanding of the programme, including candid recognition of the problems. Such solutions for the development of an informed populace may be found in connexion with the growing trend for "consumerism" (i.e., consumers acting to protect their own interests) to be applied to matters of health in positive ways and not simply in unjustified liability litigation as has sometimes been the case. Individuals are assuming greater responsibility for understanding their own medical problems, are attempting to take a greater role in maintaining their own health, and are no longer expecting infallible magic from their physicians. In an extension of this development and of the increased information becoming available to the public, contributions could be made by the medical and scientific community, by government health agencies, and by the media towards a far more realistic public awareness of the risks and benefits entailed in any mass vaccination programme. When millions of persons receive a vaccine, properly prepared and administered for the protection of the nation's health, a very small number of individuals may experience atypical adverse reactions. In effect, these individuals pay the whole price for the benefits provided to the general population. If the public recognizes and accepts the small risks as being worthwhile when balanced against the large benefits of vaccination, or when compared to far larger risks to the whole population if the vaccine were not given, more responsible attitudes should result. First, public concern and private litigation should become tempered. Second, the public should be willing to accept its share of the programme's human cost; those protected should certainly be prepared to bear the financial burden of those few individuals who might be harmed by the programme, and thus be willing to provide support and assistance from taxation for the victims or their families.

Six countries already have such a scheme: Denmark, the Federal Republic of Germany, Hungary, Japan, Monaco, and Switzerland. In 1976 and 1977, recommendations were made towards meeting some of these problems in the USA as well. Liability for losses sustained by individuals who are believed to be vaccine recipients or contacts should be assumed by the government, and appropriate expert committees should be established to review claims and assess their validity.

A converse proposition ought also to be considered: if government policy keeps life-saving vaccines from the public, because of negligence, political opportunism, fear of making responsible decisions, ignorance, or merely inertia, the government should then bear the costs of the illnesses that would have been prevented had the vaccines been used.
